AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions and listings of claims in the application:

LISTING OF CLAIMS:

1. (original): A set of genetic polymorphisms being associated with optic neuropathy, which comprises at least one polymorphism selected from the group consisting of:

(1) AAG to AAT substitution at codon 198 of the Endothelin-1 gene (Lys198Asn);

(2) -1370T>G polymorphism of the Endothelin-1 gene promoter region;

(3) A138 insertion/deletion(A138I/D) polymorphism in exon 1 of the Endothelin-1 gene;

(4) +70C>G polymorphism in 3' non-coding region of the Endothelin receptor A gene;

(5) +1222C>T polymorphism of the Endothelin Receptor A gene;

(6) CAC to CAT substitution at codon 323 in exon 6 of the Endothelin Receptor A gene (His323His);

(7) -231A>G polymorphism of the Endothelin Receptor A gene promoter region;

(8) CTG to CTA substitution at codon 277 in exon 4 of the Endothelin receptor B gene;

(9) 9099C>A polymorphism of the Mitochondrial gene;

(10) 9101T>G polymorphism of the Mitochondrial gene;

(11) 9101T>C polymorphism of the Mitochondrial gene;

(12) 9804G>A polymorphism of the Mitochondrial gene;

(13) 11778G>A polymorphism of the Mitochondrial gene;

(14) -713T>G polymorphism of the Angiotensin II type 1 receptor gene promoter region;

(16) 3123C>A polymorphism of the Angiotensin II type 2 receptor gene;

(25) CAA to CGA substitution at codon 192 of the Paraoxonase 1 gene (Gln192Arg);

(26) TTG to ATG substitution at codon 55 of the Paraoxonase 1 gene (Leu55Met);

(27) CGG to CAG substitution at codon 144 of the Noelin 2 gene (Arg144Gln);

(32) GGA to CGA substitution at codon 389 of the β1 adrenergic receptor gene (Gly389Arg);

(35) 1105T>C polymorphism of the Myocilin gene (Phe369Leu);

(36) 412G>A polymorphism of the Optineurin gene;

(37) 1402C>T polymorphism of the E-Selectin gene;

(38) The combination of polymorphisms of -857C>T of the Tumor necrosis factor α gene promoter region and 412G>A of the Optineurin gene;

(39) The combination of polymorphisms of -863C>A of the Tumor necrosis factor α gene promoter region and 603T>A of the Optineurin gene;

(40) CGC to CCC substitution at codon 72 of the TP53 gene (Arg72Pro);

(41) TAC to CAC substitution at codon 113 of the Microsomal epoxide hydrase1 gene (Tyr113His);

(42) -110A>C polymorphism of the Heatshock protein 70-1 gene promoter region;

(43) -338C>A polymorphism of the Endothelin converting enzyme gene promoter region;

(44) -670A>G polymorphism of the CD95 gene promoter region;

(45) AAG to AAA substitution at codon 119 of the Microsomal epoxide hydrase 1 gene(Lys119Lys);

(47) GGA to AGA substitution at codon 16 of the β2 adrenergic receptor gene (Gly16Arg); and

(48) CAA to GAA substitution at codon 27 of the β2 adrenergic receptor gene (Gln27Glu).

2. (original): A method for diagnosing or predicting susceptibility to optic neuropathy in a human subject, which comprising the steps of:

i) obtaining a biological sample from the subject,

ii) determining genotype of the sample in respect of the set of the polymorphisms of claim 1, and

iii) diagnosing or predicting susceptibility to optic neuropathy in the subject based on the genotype.

3. (original): The method of Claim 2, wherein the optic neuropathy is glaucoma or Leber's disease.

4. (original): The method of Claim 2, wherein the set of polymorphisms further comprises at least one genetic polymorphism which has been known to be associated with optic neuropathy.

5. (original): A method for diagnosing or predicting susceptibility to glaucoma in a human subject, which comprising the steps of:

i) obtaining a biological sample from the subject,

ii) determining genotype of the sample in respect of a set of polymorphisms comprising at least one polymorphism selected from the group consisting of:

(1) AAG to AAT substitution at codon 198 of the Endothelin-1 gene (Lys198Asn);

(2) -1370T>G polymorphism of the Endothelin-1 gene promoter region;

(3) A138 insertion/deletion(A138I/D) polymorphism in exon 1 of the Endothelin-1 gene;

(4) +70C>G polymorphism in 3' non-coding region of the Endothelin receptor A gene;

(5) +1222C>T polymorphism of the Endothelin Receptor A gene;

(6) CAC to CAT substitution at codon 323 in exon 6 of the Endothelin Receptor A gene (His323His);

(7) -231A>G polymorphism of the Endothelin Receptor A gene promoter region;

(8) CTG to CTA substitution at codon 277 in exon 4 of the Endothelin receptor B gene;

(9) 9099C>A polymorphism of the Mitochondrial gene;

(10) 9101T>G polymorphism of the Mitochondrial gene;

(11) 9101T>C polymorphism of the Mitochondrial gene;

(12) 9804G>A polymorphism of the Mitochondrial gene;

(13) 11778G>A polymorphism of the Mitochondrial gene;

(14) -713T>G polymorphism of the Angiotensin II type 1 receptor gene promoter region;

(16) 3123C>A polymorphism of the Angiotensin II type 2 receptor gene;

(25) CAA to CGA substitution at codon 192 of the Paraoxonase 1 gene (Gln192Arg);

(26) TTG to ATG substitution at codon 55 of the Paraoxonase 1 gene (Leu55Met);

(27) CGG to CAG substitution at codon 144 of the Noelin 2 gene (Arg144Gln);

(32) GGA to CGA substitution at codon 389 of the β1 adrenergic receptor gene (Gly389Arg);

(35) 1105T>C polymorphism of the Myocilin gene (Phe369Leu);

(36) 412G>A polymorphism of the Optineurin gene;

(37) 1402C>T polymorphism of the E-Selectin gene;

(38) The combination of polymorphisms of -857C>T of the Tumor necrosis factor α gene promoter region and 412G>A of the Optineurin gene;

(39) The combination of polymorphisms of -863C>A of the Tumor necrosis factor α gene promoter region and 603T>A of the Optineurin gene;

(42) -110A>C polymorphism of the Heatshock protein 70-1 gene promoter region;

(43) -338C>A polymorphism of the Endothelin converting enzyme gene promoter region;

(44) -670A>G polymorphism of the CD95 gene promoter region;

(45) AAG to AAA substitution at codon 119 of the Microsomal epoxide hydrase 1 gene(Lys119Lys);

(47) GGA to AGA substitution at codon 16 of the β2 adrenergic receptor gene (Gly16Arg); and

(48) CAA to GAA substitution at codon 27 of the β2 adrenergic receptor gene (Gln27Glu), and

iii) diagnosing or predicting susceptibility to glaucoma in the subject based on the genotype.

6. (original): The method of Claim 5, wherein the set of polymorphisms further comprises at least one genetic polymorphism which has been known to be associated with glaucoma.

7. (original): The method of Claim 5, wherein the at least one genetic polymorphism is selected from the group consisting of:

(1) AAG to AAT substitution at codon 198 of the Endothelin-1 gene (Lys198Asn);

(2) -1370T>G polymorphism of the Endothelin-1 gene promoter region;

(5) +1222C>T polymorphism of the Endothelin Receptor A gene;

(6) CAC to CAT substitution at codon 323 in exon 6 of the Endothelin Receptor A gene (His323His);

(7) -231A>G polymorphism of the Endothelin Receptor A gene promoter region;

(16) 3123C>A polymorphism of the Angiotensin II type 2 receptor gene;

(26) TTG to ATG substitution at codon 55 of the Paraoxonase 1 gene (Leu55Met);

(32) GGA to CGA substitution at codon 389 of the β1 adrenergic receptor gene (Gly389Arg);

(43) -338C>A polymorphism of the Endothelin converting enzyme gene promoter region;

(45) AAG to AAA substitution at codon 119 of the Microsomal epoxide hydrase 1 gene(Lys119Lys), and

the glaucoma is normal tension glaucoma.

8. (original): The method of Claim 7, wherein the set of polymorphisms further comprises at least one genetic polymorphism which has been known to be associated with normal tension glaucoma.

9. (original): The method of Claim 5 wherein the at least one genetic polymorphism is selected from the group consisting of

(4) +70C>G polymorphism in 3' non-coding region of the Endothelin receptor A gene;

(14) -713T>G polymorphism of the Angiotensin II type 1 receptor gene promoter region;

(25) CAA to CGA substitution at codon 192 of the Paraoxonase 1 gene (Gln192Arg);

(35) 1105T>C polymorphism of the Myocilin gene (Phe369Leu);

(36) 412G>A polymorphism of the Optineurin gene;

(38) The combination of polymorphisms of -857C>T of the Tumor necrosis factor α gene promoter region and 412G>A of the Optineurin gene;

(42) -110A>C polymorphism of the Heatshock protein 70-1 gene promoter region;

(44) -670A>G polymorphism of the CD95 gene promoter region;

(47) GGA to AGA substitution at codon 16 of the β2 adrenergic receptor gene (Gly16Arg); and

(48) CAA to GAA substitution at codon 27 of the β2 adrenergic receptor gene (Gln27Glu), and the glaucoma is primary open angle glaucoma.

10. (original): The method of Claim 9, wherein the set of polymorphisms further comprises at least one genetic polymorphism which has been known to be associated with primary open angle glaucoma.

11. (original): A method for diagnosing or predicting susceptibility to Leber's disease in a human subject, which comprising the steps of:

i) obtaining a biological sample from the subject,

ii) determining genotype of the sample in respect of the set of the polymorphisms comprising at least one polymorphism selected from the group consisting of:

(40) CGC to CCC substitution at codon 72 of the TP53 gene (Arg72Pro); and

(41) TAC to CAC substitution at codon 113 of the Microsomal epoxide hydrase1 gene (Tyr113His), and

iii) diagnosing or predicting susceptibility to Leber's disease in the subject based on the genotype.

12. (original): The method of Claim 11, wherein the set of polymorphisms further comprises at least one genetic polymorphism which has been known to be associated with Leber's disease.

13. (currently amended): The method of Claim 2~~any of Claims 2-12~~, wherein the genotype is determined by the method selected from the group consisting of polymerase chain reaction restriction fragment length polymorphism (PCR-RFLP) analysis, polymerase chain reaction followed by single strand conformation polymorphism (PCR-SSCP) analysis, ASO hybridization analysis, direct sequencing analysys, ARMS analysis, DGGE analysis, RNseA cleaving analysis, chemical restriction analysis, DPL analysis, TaqMan® PCR analysis, Invader® assay, MALDI-TOF/MS analysis, TDI analysis, single nucleotide extension assay, WAVE assay and one molecular fluorescent detection assay, and a mixture thereof.

14. (original): A kit for diagnosing or predicting susceptibility to optic neuropathy in a human subject which comprises primer set and/or probe suitable for determining genotype in respect of

a set of genetic polymorphisms comprising at least one genetic polymorphism selected from the group consisting of:

(1) AAG to AAT substitution at codon 198 of the Endothelin-1 gene (Lys198Asn);

(2) -1370T>G polymorphism of the Endothelin-1 gene promoter region;

(3) A138 insertion/deletion(A138I/D) polymorphism in exon 1 of the Endothelin-1 gene;

(4) +70C>G polymorphism in 3' non-coding region of the Endothelin receptor A gene;

(5) +1222C>T polymorphism of the Endothelin Receptor A gene;

(6) CAC to CAT substitution at codon 323 in exon 6 of the Endothelin Receptor A gene (His323His);

(7) -231A>G polymorphism of the Endothelin Receptor A gene promoter region;

(8) CTG to CTA substitution at codon 277 in exon 4 of the Endothelin receptor B gene;

(9) 9099C>A polymorphism of the Mitochondrial gene;

(10) 9101T>G polymorphism of the Mitochondrial gene;

(11) 9101T>C polymorphism of the Mitochondrial gene;

(12) 9804G>A polymorphism of the Mitochondrial gene;

(13) 11778G>A polymorphism of the Mitochondrial gene;

(14) -713T>G polymorphism of the Angiotensin II type 1 receptor gene promoter region;

(16) 3123C>A polymorphism of the Angiotensin II type 2 receptor gene;

(25) CAA to CGA substitution at codon 192 of the Paraoxonase 1 gene (Gln192Arg);

(26) TTG to ATG substitution at codon 55 of the Paraoxonase 1 gene (Leu55Met);

(27) CGG to CAG substitution at codon 144 of the Noelin 2 gene (Arg144Gln);

(32) GGA to CGA substitution at codon 389 of the β1 adrenergic receptor gene (Gly389Arg);

(35) 1105T>C polymorphism of the Myocilin gene (Phe369Leu);

(36) 412G>A polymorphism of the Optineurin gene;

(37) 1402C>T polymorphism of the E-Selectin gene;

(38) The combination of polymorphisms of -857C>T of the Tumor necrosis factor α gene promoter region and 412G>A of the Optineurin gene;

(39) The combination of polymorphisms of -863C>A of the Tumor necrosis factor α gene promoter region and 603T>A of the Optineurin gene

(40) CGC to CCC substitution at codon 72 of the TP53 gene (Arg72Pro);

(41) TAC to CAC substitution at codon 113 of the Microsomal epoxide hydrase1 gene (Tyr113His);

(42) -110A>C polymorphism of the Heatshock protein 70-1 gene promoter region;

(43) -338C>A polymorphism of the Endothelin converting enzyme gene promoter region;

(44) -670A>G polymorphism of the CD95 gene promoter region;

(45) AAG to AAA substitution at codon 119 of the Microsomal epoxide hydrase 1 gene(Lys119Lys);

(47) GGA to AGA substitution at codon 16 of the β2 adrenergic receptor gene (Gly16Arg); and

(48) CAA to GAA substitution at codon 27 of the β2 adrenergic receptor gene (Gln27Glu).

15. (original): The kit of Claim 14, wherein the optic neuropathy is glaucoma or Leber's disease.

16. (original): The kit of Claim 14, wherein the set of the genetic polymorphisms further comprises at least one genetic polymorphism which has been known to be associated with optic neuropathy.

17. (original): A kit for diagnosing or predicting susceptibility to glaucoma in a human subject which comprises primer set and/or probe suitable for determining genotype in respect of a set of genetic polymorphisms comprising at least one genetic polymorphism selected from the group consisting of:

(1) AAG to AAT substitution at codon 198 of the Endothelin-1 gene (Lys198Asn);

(2) -1370T>G polymorphism of the Endothelin-1 gene promoter region;

(3) A138 insertion/deletion(A138I/D) polymorphism in exon 1 of the Endothelin-1 gene;

(4) +70C>G polymorphism in 3' non-coding region of the Endothelin receptor A gene;

(5) +1222C>T polymorphism of the Endothelin Receptor A gene;

(6) CAC to CAT substitution at codon 323 in exon 6 of the Endothelin Receptor A gene (His323His);

(7) -231A>G polymorphism of the Endothelin Receptor A gene promoter region;

(8) CTG to CTA substitution at codon 277 in exon 4 of the Endothelin receptor B gene;

(9) 9099C>A polymorphism of the Mitochondrial gene;

(10) 9101T>G polymorphism of the Mitochondrial gene;

(11) 9101T>C polymorphism of the Mitochondrial gene;

(12) 9804G>A polymorphism of the Mitochondrial gene;

(13) 11778G>A polymorphism of the Mitochondrial gene;

(14) -713T>G polymorphism of the Angiotensin II type 1 receptor gene promoter region;

(16) 3123C>A polymorphism of the Angiotensin II type 2 receptor gene;

(25) CAA to CGA substitution at codon 192 of the Paraoxonase 1 gene (Gln192Arg);

(26) TTG to ATG substitution at codon 55 of the Paraoxonase 1 gene (Leu55Met);

(27) CGG to CAG substitution at codon 144 of the Noelin 2 gene (Arg144Gln);

(32) GGA to CGA substitution at codon 389 of the β1 adrenergic receptor gene (Gly389Arg);

(35) 1105T>C polymorphism of the Myocilin gene (Phe369Leu);

(36) 412G>A polymorphism of the Optineurin gene;

(37) 1402C>T polymorphism of the E-Selectin gene;

(38) The combination of polymorphisms of -857C>T of the Tumor necrosis factor α gene promoter region and 412G>A of the Optineurin gene;

(39) The combination of polymorphisms of -863C>A of the Tumor necrosis factor α gene promoter region and 603T>A of the Optineurin gene;

(42) -110A>C polymorphism of the Heatshock protein 70-1 gene promoter region;

(43) -338C>A polymorphism of the Endothelin converting enzyme gene promoter region;

(44) -670A>G polymorphism of the CD95 gene promoter region;

(45) AAG to AAA substitution at codon 119 of the Microsomal epoxide hydrase 1 gene(Lys119Lys);

(47) GGA to AGA substitution at codon 16 of the β2 adrenergic receptor gene (Gly16Arg); and

(48) CAA to GAA substitution at codon 27 of the β2 adrenergic receptor gene (Gln27Glu).

18. (original): The kit of Claim 17, wherein the set of the genetic polymorphisms further comprises at least one genetic polymorphism which has been known to be associated with optic neuropathy.

19. (original): A kit for diagnosing or predicting susceptibility to normal tension glaucoma in a human subject which comprises primer set and/or probe suitable for determining genotype in respect of a set of genetic polymorphisms comprising at least one genetic polymorphism selected from the group consisting of:

(1) AAG to AAT substitution at codon 198 of the Endothelin-1 gene (Lys198Asn);

(2) -1370T>G polymorphism of the Endothelin-1 gene promoter region;

(5) +1222C>T polymorphism of the Endothelin Receptor A gene;

(6) CAC to CAT substitution at codon 323 in exon 6 of the Endothelin Receptor A gene (His323His);

(7) -231A>G polymorphism of the Endothelin Receptor A gene promoter region;

(16) 3123C>A polymorphism of the Angiotensin II type 2 receptor gene;

(26) TTG to ATG substitution at codon 55 of the Paraoxonase 1 gene (Leu55Met);

(32) GGA to CGA substitution at codon 389 of the β1 adrenergic receptor gene (Gly389Arg);

(43) -338C>A polymorphism of the Endothelin converting enzyme gene promoter region;

(45) AAG to AAA substitution at codon 119 of the Microsomal epoxide hydrase 1 gene(Lys119Lys).

20. (original): The kit of Claim 19, wherein the set of the genetic polymorphisms further comprises at least one genetic polymorphism which has been known to be associated with normal tension glaucoma.

21. (original): A kit for diagnosing or predicting susceptibility to primary open angle glaucoma in a human subject which comprises primer set and/or probe suitable for determining genotype in respect of a set of genetic polymorphisms comprising at least one genetic polymorphism selected from the group consisting of:

(4) +70C>G polymorphism in 3' non-coding region of the Endothelin receptor A gene;

(14) -713T>G polymorphism of the Angiotensin II type 1 receptor gene promoter region;

(25) CAA to CGA substitution at codon 192 of the Paraoxonase 1 gene (Gln192Arg);

(35) 1105T>C polymorphism of the Myocilin gene (Phe369Leu);

(36) 412G>A polymorphism of the Optineurin gene;

(38) The combination of polymorphisms of -857C>T of the Tumor necrosis factor α gene promoter region and 412G>A of the Optineurin gene;

(42) -110A>C polymorphism of the Heatshock protein 70-1 gene promoter region;

(44) -670A>G polymorphism of the CD95 gene promoter region;

(47) GGA to AGA substitution at codon 16 of the β2 adrenergic receptor gene (Gly16Arg); and

(48) CAA to GAA substitution at codon 27 of the β2 adrenergic receptor gene (Gln27Glu).

22. (original): The kit of claim 21, wherein the set of the genetic polymorphisms further comprises at least one genetic polymorphism which has been known to be associated with primary open angle glaucoma.

23. (original): A kit for diagnosing or predicting susceptibility to Leber's disease in a human subject which comprises primer set and/or probe suitable for determining genotype in respect of a set of genetic polymorphisms comprising at least one genetic polymorphism selected from the group consisting of:

(40) CGC to CCC substitution at codon 72 of the TP53 gene (Arg72Pro);

(41) TAC to CAC substitution at codon 113 of the Microsomal epoxide hydrase1 gene (Tyr113His).

24. (original): The kit of Claim 23, wherein the set of the genetic polymorphisms further comprises at least one genetic polymorphism which has been known to be associated with Leber's disease.

25. (original): An isolated polynucleotide consisting of a segment of the sequence:

8881 tctaagatta aaaatgccct agcccacttc ttaccacaag gcacacctac accccttatc

8941 cccatactag ttattatcga aaccatcagc ctactcattc aaccaatagc cctggccgta

9001 cgcctaaccg ctaacattac tgcaggccac ctactcatgc acctaattgg aagcgccacc

9061 ctagcaatat caaccattaa ccttccctct acacttatca tcttcacaat tctaattcta

9121 ctgactatcc tagaaatcgc tgtcgcctta atccaagcct acgttttcac acttctagta

9181 agcctctacc tgcacgacaa cacataatga cccaccaatc acatgcctat catatagtaa

wherein the segment comprises at least 90 contignuous nucleotide, and the at least 90 contignuous nucleotide includes position 9099 of the sequence, and wherein position 9099 of the sequence is A, or an isolated polynucleotide which is entirely complementary to the above segment.

26 (original): An isolated polynucleotide consisting of a segment of the sequence as shown in Claim 25, wherein the segment comprises at least 90 contignuous nucleotide, and the at least 90 contignuous nucleotide includes position 9101 of the sequence, and wherein position 9101 of the sequence is G, or an isolated polynucleotide which is entirely complementary to the above segment.

27. (original): An isolated polynucleotide consisting of a segment of the sequence:

301 actggaaagc acgggtgctg tggtgtactc ggggagcctc tatttccagg gcgctgagtc

361 cagaactgtc ataagatatg agctgaatac cgagacagtg aaggctgaga aggaaatccc

421 tggagctggc taccacggac agttcccgta ttcttggggt ggctacacgg acattgactt

481 ggctgtggat gaagcaggcc tctgggtcat ttacagcacc gatgaggcca aaggtgccat

541 tgtcctctcc aaactgaacc cagagaatct ggaactcgaa caaacctggg agacaaacat

wherein the segment comprises at least 90 contignuous nucleotide, and the at least 90 contignuous nucleotide includes codon 369, which is corresponding to the underlined nucleotides

of the sequence, and wherein codon 369 is substituted such that it codes for Leu, or an isolated polynucleotide which is entirely complementary to the above segment.

28. (original): An isolated polynucleotide consisting of a segment of the sequence:

79741 ttagttccta caatggagtc atgtctggga agaatctagg gtccaatatg agccacatgt

79801 caagggccag gtgtgcatca aagacaaagg gtgaagttat gagtcagagg ttggagtcat

79861 gtctgggtca aaggccaggg gtcaggcttg gccatggttc catcttgatg cacaggagct

79921 gaaggacagg atgacggaac tgttgcccct gagctcggtc ctggagcagt acaaggcaga

79981 cacgcggacc attgtacgct tgcgggagga ggtgaggaat ctctccggca gtctggcggc

80041 cattcaggag gagatgggtg cctacgggta tgaggacctg cagcaacggg tgatggccct

80101 ggaggcccgg ctccacgcct gcgcccagaa gctgggtatg ccttggccct tgaccctgac

80161 ccctgatctc tgactgccac acccaactcc agtatcacct gtttgtgcct agaagctgga

80221 cacagttttg acctctaact tttaaacctc aacccttgac cttcctacct aaggctacac

wherein the segment comprises at least 90 contignuous nucleotide, and the at least 90 contignuous nucleotide includes codon 144, which is corresponding to the underlined nucleotides of the sequence, and wherein codon 144 is substituted such that it codes for Gln, or an isolated polynucleotide which is entirely complementary to the above segment.

29. (original): A method for treating glaucoma in a patient who has an abnormality in the Myocilin gene, which comprises suppressing the expression of the abnormal Myocilin genes in the patient.

30. (original): The method of Claim 29, wherein the suppression is carried out by means of RNA interference method.

31. (original): A method for predicting the response of a subject to the treatment with a drug, which comprises the steps of; determining genotype in respect of at least one genetic polymorphism being associated with optic neuropathy, and predicting the response of the patient based on the genotype.

32. (original): The method of Claim 31, wherein the optic neuropathy is glaucoma or Leber's disease.

33. (original): The method of Claim 31, wherein the optic neuropathy is glaucoma.

34. (original): The method of Claim 31, wherein the at least one genetic polymorphism is 3123C>A polymorphism of the Angiotensin II type 2 receptor gene.

35. (original): The method of Claim 31, wherein the drug is an Angiotensin Receptor II antagonist.